

IN THE SPECIFICATION:

Please replace lines 23-37 on page 58 and lines 1-21 on page 59 of the previously submitted Substitute Specification with the following replacement section:

It has been shown previously that a mutant p53 with two amino acid substitutions at positions 14 and 19 retains approximately 50% transactivation activity and 60% adenovirus E1B-55kDa binding affinity, but only approximately 1% MDM2 binding affinity compared to wild type p53 (Lin et al., Genes & Dev. 8(1994):1235-1246). To construct adenoviruses according to the invention that express this mutant p53, two single nucleotide substitutions that change these amino acids (T>A, L14Q and T>G, F19C) were introduced into the p53 gene on plasmid pABS.4-p53 (see example 1) by PCR-mediated site-directed mutagenesis using Pfu polymerase (Stratagene). First, two PCR amplification products were made using (1) upstream primer 5'-CGTTTCCCGTTGAATATGGC-3' (SEQ ID NO: 1) and mutation primer 5'-CTGAACATGTTTCCTGACTCTGAGGGGGCTC-3' (SEQ. ID NO: 2) to amplify a first fragment of 651 basepairs; and (2) mutation primer 5'-CCTCAGAGTCAGGAAACATGTTTCAGACC-3' (SEQ ID NO: 3) and downstream primer 5'-GAAGTCTCATGGAAGCCAGC-3' (SEQ ID NO: 4) to amplify a second fragment of 376 basepairs from pABS.4-p53. Next, the two amplification products were mixed and amplified using the upstream and downstream primers to generate a full length 1002 basepair amplification product containing the two point-mutations. The wildtype SVE-p53 expression cassette from pABS.4-p53 was subcloned into the KpnI and Sall sites in the multiple cloning site of a pBluescriptSK- derivative with deleted SmaI restriction site to create pBSKΔSma-p53. The 568 bp KpnI/SmaI fragment from the 1002 basepair PCR product encompassing the two mutations was used to replace the corresponding wild type p53 fragment in pBSKΔSma-p53, creating pBSKΔSma-p53mut14/19. Correct introduction of the two nucleotide substitutions without any other changes in the p53 gene sequence were confirmed by DNA sequencing (performed at Baseclear in Leiden, the Netherlands). The SVE-p53mut14/19 expression cassette from pBSKΔSma-p53mut14/19 was cloned into KpnI/Sall-digested pABS.4(Microbix) to

create pABS.4-p53mut14/19. Functional p53-specific transactivation capacity by the pABS.4-p53mut14/19 encoded mutant p53 was analyzed by p53-specific transactivation assay. A sequence listing is provided herewith.